

**INTERNATIONAL SEARCH REPORT**

International Application No PCT/EP2004/008609
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b>
IPC 7 C07K1/22 C07K1/32 C07K14/47 C07K14/74 G01N33/569 A61K38/00 A61K39/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE Geneseq 'Online! 29 January 2004 (2004-01-29), "Human Protein P13284, SEQ ID NO 10787." XP002305086 retrieved from EBI accession no. GSN:ADD45354 Database accession no. ADD45354 abstract &amp; WO 03/016475 A (BAYER AG ; D URSO DONATELLA (DE); BEFORT KATIA (FR); GEN HOSPITAL CORP) 27 February 2003 (2003-02-27)</p> <p style="text-align: center;">-/-</p>	17,18, 23,29

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

1 February 2005

Date of mailing of the international search report

21.02.05

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE Geneseq 'Online!'            22 April 2004 (2004-04-22), "Human apoptosis-associated protein SEQ ID 154."            XP002304913            retrieved from EBI accession no.            GSN:ADI62711            Database accession no. ADI62711            abstract            &amp; WO 03/058021 A (XANTOS BIOMEDICINE AG ; KESPER BJOERN (DE); SCHAEFER ROLF (DE); KAZINS) 17 July 2003 (2003-07-17)            claim 48</p> <p>-----</p> <p>WO 93/18153 A1 (SMITH, GEOFFREY, LILLEY)            16 September 1993 (1993-09-16)            page 9, line 28 - page 10, line 2; figures 2, cont.            page 20, line 12 - line 17            -&amp; DATABASE EPO Proteins 'Online!            19 October 1999 (1999-10-19), "Sequence 25 from Patent WO9318153."            XP002315336            retrieved from EBI accession no.            EPOP:A76385            Database accession no. A76385            -&amp; DATABASE EPO Proteins 'Online!            19 October 1999 (1999-10-19), "Sequence 34 from Patent WO9318153."            XP002315337            retrieved from EBI accession no.            EPOP:A76394            Database accession no. A76394</p> <p>-----</p> <p>DATABASE Geneseq 'Online!            19 August 2002 (2002-08-19), "Human peptide encoded by genome-derived single exon probe SEQ ID 30218."            XP002315338            retrieved from EBI accession no.            GSN:ABG40553            Database accession no. ABG40553            the whole document            &amp; WO 01/86003 A2 (MOLECULAR DYNAMICS, INC., USA) 15 November 2001 (2001-11-15)</p> <p>-----</p> <p>DI BARTOLO, V. ET AL: "Binding of human GM-CSF to synthetic peptides of the alpha subunit of its receptor"            JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH , 16(1 &amp; 2), 77-92            CODEN: JRETET; ISSN: 1079-9893, 1996,            XP009043176            page 79 - page 80; table 1            page 89 - page 90</p> <p>-----</p> <p>-/-</p>	17,18, 23,28,29
X		1,10, 15-19
X		1,10, 15-19
X		1,12, 15-19

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CARR P D ET AL: "Structure of the complete extracellular domain of the common beta subunit of the human GM-CSF, IL-3, and IL-5 receptors reveals a novel dimer configuration." CELL. 26 JAN 2001, vol. 104, no. 2, 26 January 2001 (2001-01-26), pages 291-300, XP002315334 ISSN: 0092-8674 the whole document</p> <p>-----</p> <p>TSARK ELEANOR C ET AL: "Differential MHC class II-mediated presentation of rheumatoid arthritis autoantigens by human dendritic cells and macrophages." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 1 DEC 2002, vol. 169, no. 11, 1 December 2002 (2002-12-01), pages 6625-6633, XP002304908 ISSN: 0022-1767 cited in the application the whole document</p> <p>-----</p> <p>SANTAMBROGIO L ET AL: "Extracellular antigen processing and presentation by immature dendritic cells" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 96, no. 26, 21 December 1999 (1999-12-21), pages 15056-15061, XP002222004 ISSN: 0027-8424</p> <p>-----</p> <p>FRIEDE T ET AL: "Natural ligand motifs of closely related HLA-DR4 molecules predict features of rheumatoid arthritis associated peptides." BIOCHIMICA ET BIOPHYSICA ACTA. 7 JUN 1996, vol. 1316, no. 2, 7 June 1996 (1996-06-07), pages 85-101, XP002304909 ISSN: 0006-3002</p> <p>-----</p> <p>DONGRE A R ET AL: "In vivo MHC class II presentation of cytosolic proteins revealed by rapid automated tandem mass spectrometry and functional analyses." EUROPEAN JOURNAL OF IMMUNOLOGY. MAY 2001, vol. 31, no. 5, May 2001 (2001-05), pages 1485-1494, XP002304910 ISSN: 0014-2980 cited in the application</p> <p>-----</p>	12
		-/-

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHICZ R M ET AL: "SPECIFICITY AND PROMISCUITY AMONG NATURALLY PROCESSED PEPTIDES BOUND TO HLA-DR ALLELES" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 178, no. 1, 1 July 1993 (1993-07-01), pages 27-47, XP002069888 ISSN: 0022-1007 cited in the application</p> <p>-----</p>	
A	<p>ARUNACHALAM B ET AL: "Intracellular formation and cell surface expression of a complex of an intact lysosomal protein and MHC class II molecules." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 15 JUN 1998, vol. 160, no. 12, 15 June 1998 (1998-06-15), pages 5797-5806, XP002304911 ISSN: 0022-1767</p> <p>-----</p>	
A	<p>DATABASE UniProt 'Online! 1 November 1996 (1996-11-01), "Cytokine receptor complex common beta chain h beta c (Fragment)." XP002315339 retrieved from EBI accession no. UNIPROT:Q63968 Database accession no. Q63968</p> <p>-----</p>	
A	<p>CANTAGREL A ET AL: "Interleukin-1beta, interleukin-1 receptor antagonist, interleukin-4, and interleukin-10 gene polymorphisms: relationship to occurrence and severity of rheumatoid arthritis." ARTHRITIS AND RHEUMATISM. JUN 1999, vol. 42, no. 6, June 1999 (1999-06), pages 1093-1100, XP002315335 ISSN: 0004-3591</p> <p>-----</p>	
A	<p>RAMMENSEE H-G ET AL: "MHC LIGANDS AND PEPTIDE MOTIFS: FIRST LISTING" IMMUNOGENETICS, SPRINGER VERLAG, BERLIN, DE, vol. 41, no. 4, February 1995 (1995-02), pages 178-228, XP000673045 ISSN: 0093-7711</p> <p>-----</p>	

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

2,10,12 (complete), 1, 14-19, 23-28, 29 (partially)

4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 2 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from Interferon-gamma-inducible lysosomal thiol reductase (GILT, SEQ ID NOs: 1-3, 49); use of GILT as a marker for rheumatoid arthritis (SEQ ID NO: 40)  
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Invention 2: claims 3 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from Integrin beta-2 (SEQ ID NOs: 58, 59, 103); use of integrin beta-2 as a marker for rheumatoid arthritis (SEQ ID NO: 123)  
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Inventions 3-29: claims 4-13, 27 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from phosphatidylinositol-4,5-bisphosphate 3-kinase (SEQ ID NO: 60, 104), urokinase-type plasminogen activator (SEQ ID NO: 61, 105), immunoglobulin heavy chain V-III region (SEQ ID NO: 62, 106), DJ-1 protein (SEQ ID NO: 63, 107), apolipoprotein B-100 (SEQ ID NO: 4, 5, 50), 26S proteasome non-ATPase regulatory subunit 8 (SEQ ID NO: 64, 108), Interleukin-1 receptor (SEQ ID NO: 68, 109), fibromodulin (SEQ ID NO: 69, 70, 110), GM-CSF/IL-3/IL-5 receptor (SEQ ID NO: 71, 72, 111), sorting nexin 3 (SEQ ID NO: 73, 112), inter-alpha-trypsin inhibitor heavy chain H4 (SEQ ID NO: 6-12, 51), complement C4 (SEQ ID NO: 13-18, 52), complement C3 alpha chain (SEQ ID NO: 19-23, 74, 75, 53), complement C3 beta chain (SEQ ID NO: 76, 77, 113), SH3 domain-binding glutamic acid-rich-like protein 3 (SEQ ID NO: 24-27, 54), interleukin-4 induced protein 1 (SEQ ID NO: 28-30, 55), hemopexin (SEQ ID NO: 31-35, 78, 56), Hsc70-interacting protein (SEQ ID NO: 36-39, 57), invariant chain (Ii) (SEQ ID NO: 79-83, 114), retinoic acid receptor responder protein 2 (SEQ ID NO: 84-86, 115), fibronectin (SEQ ID NO: 87-91, 116), cathepsin B (SEQ ID NO: 92, 117), tripeptidyl-peptidase II (SEQ ID NO: 93, 94, 118), legumain (SEQ ID NO: 95, 119), platelet activating factor receptor (SEQ ID NO: 96, 120), poly-alpha-2,8-sialyltransferase (SEQ ID NO: 97, 121), ras-related protein Rab-11B (SEQ ID NO: 98-102, 122); use of said polypeptides as markers for rheumatoid arthritis (SEQ ID NO: 41-48, 124-141)  
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Invention 30: claims 20-22

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

method for isolating and identifying MHC class II associated  
RA antigenic peptides

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**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No	
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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 03016475	A	27-02-2003	CA	2457819 A1		27-02-2003
			EP	1478772 A2		24-11-2004
			WO	03016475 A2		27-02-2003
WO 03058021	A	17-07-2003	AU	2003235789 A1		24-07-2003
			WO	03058021 A2		17-07-2003
WO 9318153	A1	16-09-1993	AU	3641893 A		05-10-1993
			EP	0656949 A1		14-06-1995
WO 0186003	A2	15-11-2001	AU	3087801 A		14-08-2001
			AU	3087901 A		14-08-2001
			AU	3088001 A		14-08-2001
			AU	3088101 A		14-08-2001
			AU	3088201 A		14-08-2001
			AU	3088301 A		14-08-2001
			AU	3275701 A		14-08-2001
			AU	3275801 A		20-11-2001
			AU	3275901 A		14-08-2001
			AU	3276001 A		14-08-2001
			AU	3311401 A		14-08-2001
			AU	3658901 A		14-08-2001
			AU	6343201 A		11-12-2001
			AU	9295701 A		02-04-2002
			EP	1309723 A2		14-05-2003
			EP	1309724 A2		14-05-2003
			EP	1292704 A2		19-03-2003
			EP	1325149 A2		09-07-2003
			EP	1292705 A2		19-03-2003
			EP	1290216 A2		12-03-2003
			EP	1341930 A2		10-09-2003
			EP	1332224 A2		06-08-2003
			EP	1325150 A2		09-07-2003
			EP	1309725 A2		14-05-2003
			EP	1290217 A2		12-03-2003
			GB	2361238 A , B		17-10-2001
			GB	2373500 A , B		25-09-2002
			GB	2374929 A		30-10-2002
			GB	2383043 A		18-06-2003
			GB	2375539 A , B		20-11-2002
			GB	2375111 A , B		06-11-2002
			GB	2374872 A		30-10-2002
			GB	2378754 A , B		19-02-2003
			GB	2382814 A , B		11-06-2003
			GB	2385053 A , B		13-08-2003
			GB	2376018 A		04-12-2002
			GB	2376237 A		11-12-2002
			GB	2380197 A		02-04-2003
			GB	2396351 A , B		23-06-2004
			GB	2396352 A , B		23-06-2004
			GB	2397376 A , B		21-07-2004
			JP	2004501617 T		22-01-2004
			WO	0157270 A2		09-08-2001
			WO	0157271 A2		09-08-2001
			WO	0157272 A2		09-08-2001
			WO	0157273 A2		09-08-2001
			WO	0157274 A2		09-08-2001
			WO	0157275 A2		09-08-2001

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0186003	A2	WO 0157276 A2	09-08-2001